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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,867	03/15/2000	Henry Yue	PF-0678US	9574

27904 7590 06/23/2003

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/525,867	YUE ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 May 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *29 May 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6.☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *3-6 and 8*.

Claim(s) objected to: *none*.

Claim(s) rejected: *31*.

Claim(s) withdrawn from consideration: *10-14, 23, 26-30, 32-36*.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *PTO-892*

ADVISORY ACTION

Status of the Application

1. Claims 3-6, 8, 10-14, 23, 26-36 are pending.

2. The request for entering amendments to claims 3-6, 8 and 31, cancellation of claims 24-25, and arguments filed on 5/29/2003 under 37 CFR 1.116 in reply to the Final Action Paper No. 13 mailed on 2/24/2003 are acknowledged. The proposed amendments will be entered since they are deemed sufficient to overcome objections previously applied. However, entry of these amendments is not deemed sufficient to place the application in condition for allowance for the reasons set forth below.

3. As indicated in previous Office Action Paper No. 13, claims 10-14, 23, 26-30, 32-36 were withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Since these claims have not been canceled, claims 10-14, 23, 26-30, 32-36 remain withdrawn from further consideration.

4. Applicant's submission of a declaration under 37 CFR 1.132 by Tod Bedilion is acknowledged. It is noted however that the declaration is not properly executed since it has not been signed and dated. Furthermore, the declaration was not submitted in response to issues first raised by the Examiner in the Final Action, it was not timely presented, and even if signed, it would have not been considered by the Examiner.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

5. Claim 31 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection has been discussed at length in Paper No. 13, mailed on 2/24/2003.

6. **In page 9-11**, Applicants argue that "function" is not required to describe and use the claimed polynucleotides and that the Examiner has not provided evidence or sound scientific reasoning to support the allegation of lack of written description. Applicants submit that the last Office Action (Paper No. 13) should not have been made final since the instant rejection as applied to claim 31 appears to be a new rejection as it was not applied to claim 10 in the Office Action mailed on 3/12/2002 (Paper No. 9). Applicants assert that according to case law and the PTO's own Guidelines for Examination of Patent Applications under 35 USC 112, first paragraph, the written description requirement is fulfilled by what is known or conventional in the art and what is specifically disclosed in the specification. Applicants argue that there is no requirement that the claims recite a particular function since they claims already provide sufficient structural definition of the polynucleotides claimed. As such, the Examiner's position is a misguided attempt to limit the scope of Applicant's invention.

7. Applicant's arguments have been considered but are not deemed persuasive. The Examiner disagrees with Applicant's contention that (1) function is not required to describe and use the claimed invention, (2) sufficient structural definition has been provided which would fulfill the written description requirement, and (3) the Examiner has not provided evidence/scientific reasoning to support her position. The claim, while reciting a structural limitation, does not recite a functional limitation. As such, the claimed polynucleotides can have any function. The specification fails to disclose other functions for the claimed polynucleotides, with the exception of that associated with the polynucleotide of SEQ ID NO: 9. The Examiner presented references which teach the unpredictability of the art in determining function based on structural homology as evidence of how the teachings of the art in combination with what is

disclosed in the specification is not sufficient to fulfill the written description requirement as set forth in the USPTO Guidelines. As indicated in previous Office Action Paper No. 13, the claim is drawn to "naturally occurring" polynucleotides, which one of skill in the art would interpret as "as found in nature". As such, allelic variants are encompassed by the instant claim. As defined by the specification (pages 6-7), allelic variants are alternative forms of a gene which may result in at least one mutation in the nucleic acid structure. These alternative forms may result in altered mRNAs or polypeptides whose structure or function may be altered. The specification is silent in regard to where these mutations may occur nor does it provide any suggestion as to how the structure of the polynucleotide of SEQ ID NO: 9 relates to the structure of any naturally occurring variant such as an allele. Furthermore, the general knowledge in the art does not provide any indication of how a naturally-occurring variant such as an allele is representative of unknown naturally-occurring variants nor there is indication in the art suggesting that the structure of one allele provides guidance as to the structure of others.

In regard to the only function disclosed in the specification, i.e. PSST subunit of the NADH:ubiquinone oxidoreductase complex, it is noted that the specification is silent in regard to the critical structural elements required to display the disclosed function, nor there is any teaching as to which are the nucleotides which can be modified (i.e. substituted, deleted or inserted) in the polynucleotide of SEQ ID NO: 9 and still encode a PSST subunit of the NADH:ubiquinone oxidoreductase complex.

In regard to Applicant's arguments traversing the finality of the last Office Action, it is noted that claim 31 was first introduced for examination in Paper No. 12, filed on 6/12/2002. As

such, the rejection made on claim 31 in Paper No. 13, was necessitated by Applicant's amendment. Thus, the finality of the last Office Action is deemed proper.

8. **In page 11, part A**, Applicants emphasize that the present claim specifically defines the claimed genus through the recitation of chemical structure. Applicants argue that the instant claim recites a structural limitation which makes the instant claim different from those of *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed Cir 1997). Specifically, Applicants argue that in *Lilly* and *Fiers,* the courts found the claims to be invalid since the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features, whereas in the instant case, the polynucleotides are defined by a structural characteristic and not by a functional characteristic. Applicants argue the Office has failed to base the written description inquiry "on whatever is now claimed" and fails to provide an appropriate analysis of the instant claim and how it differs from those of the *Lilly* and *Fiers* cases.

9. Applicant's arguments have been fully considered but are not deemed persuasive. While it is acknowledged that the current claim differs from the *Lilly* and *Fiers* cases, as discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed genus. A representative number of species means that the species that

are adequately described are representative of the entire genus. The specification discloses only a single representative species of the claimed genus, i.e., SEQ ID NO:9. Further, as stated above and evidenced by the teachings of Bork, Van de Loo et al., Broun et al., and Seffernick et al., previously cited in Paper No. 13, one of skill in the art would recognize that there is substantial variation within the structure and/or function of the genus of claimed nucleic acids. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. A skilled artisan would also recognize the unpredictability of determining the function of all the claimed nucleic acids. For inventions in an unpredictable art, adequate written description of a genus that embraces widely variant species cannot be achieved by disclosing only one species within the genus. As such, neither the description of the structure and function of SEQ ID NO:9 nor the disclosure of solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus of claimed polynucleotides

10. **In page 13, part B**, Applicants argue that the present claim does not define a genus which is large and variable. Instead, Applicants argue that the claimed genus is of narrow scope and direct the Examiner's attention to the teachings of Brenner et al. (Proc. Natl. Acad. Sci. USA 95:6073-6078, 1998). According to Applicants, Brenner et al. teaches that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. Applicants submit that in accordance to Brenner et al., naturally occurring molecules may exist which could be characterized as PSST subunits of the NADH:ubiquinone oxidoreductase complex with as little as 40% identity over at least 70 residues of SEQ ID NO: 1, since according to Applicants, Brenner (TIG 15:132-1333, 1999) et al. teaches that more than

40% identity over at least 70 residues is reliable in signifying homology between proteins. Applicants conclude that the variation encompassed by the claim, i.e. naturally occurring polynucleotides having at least 80% sequence identity to the polynucleotide of SEQ ID NO: 9, is far less than the potential variation in polypeptides having at least 40% identity over at least 70 residues of SEQ ID NO: 1, wherein said polypeptides are PSST subunits of the NADH:ubiquinone oxidoreductase complex.

11. Applicant's arguments have been fully considered but are not deemed persuasive. The Examiner disagrees with Applicant's interpretation of the teachings of Brenner et al. for the following reasons. Brenner et al. (*Proc Natl Acad Sci USA* 95:6073-6078) clearly state that their comparisons "have been assessed using proteins whose relationships are known reliably from their [three dimensional] structures and functions, as described in the SCOP database" (page 6073, Abstract). In the instant case, the genus of claimed polynucleotides is related to SEQ ID NO:9, based entirely on structure (i.e. sequence), and no 3D structural analysis of PSST subunits of the NADH:ubiquinone oxidoreductase complex has been provided or used to support Applicant's assertion that naturally occurring molecules may exist which can be characterized as PSST subunits of the NADH:ubiquinone oxidoreductase complex with as little as 40% sequence identity over at least 70 residues of the polypeptide of SEQ ID NO: 1 (encoded by the polynucleotide of SEQ ID NO: 9). While Brenner et al. compares amino acid sequences of functional polypeptides encoded by genes at different loci and suggests that 30 % sequence identity between polypeptides having the aforementioned characteristics, i.e., functional polypeptides encoded by genes at different loci, can be used to propose functional similarity of

the polypeptides, nowhere in the reference there is a suggestion that all polypeptides which share at least 30 % sequence identity over 150 amino acids will share a similar function.

In addition to the references already cited which indicate the unpredictability of assigning function based on structural homology, Brenner (TIG 15:132-133, 1999) teaches that empirical laboratory evidence is essential to know the accuracy of functional assignment (page 132, left column, second paragraph). Another example which further evidences this unpredictability is described by Witkowski et al. (Biochemistry 38:11643-11650, 1999) et al. Witkowski et al. teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Therefore, in view of the evidence presented, it is unclear as to how one of skill in the art can reliably predict function with a 30% sequence identity threshold based solely on sequence homology as asserted by Applicants.

12. **In page 14, part C**, Applicants argue that the references cited by the Examiner are not relevant to the instant claim. Applicants cite a recent Federal Circuit decision in *Boehringer Ingelheim Vetmedica, Inc. v. Schering Plough Corporation*, 65 USPQ2d 1961 (CA FC 2003). Applicants assert that the teachings of Bork support the use of sequence comparison for predicting function. Furthermore, Applicants assert that the fatty acyl hydroxylases and fatty acyl desaturases of Van de Loo et al. catalyze a similar reaction and that the reaction mechanisms of both enzymes are similar based on sequence homology between them. In regard to Broun et al., applicants argue that since the enzymatic functions described in Van de Loo et al. and Broun et al. are similar, it is not surprising that they share 67% sequence homology. Accordingly, Applicants submit that the instant references are not relevant since Applicants have

not asserted that the claimed polynucleotides encode a fatty acyl hydroxylase or a fatty acyl desaturase. In regard to Seffernick et al., Applicants argue that the two enzymes described belong to a class of bacterial amidohydrolases and therefore, they do not have a diverse function as asserted by the Examiner. Moreover, Applicants argue that since they have not asserted that the claimed polynucleotides encode bacterial aminohydrolases, this reference is irrelevant. In conclusion, it is Applicant's contention that no evidence has been presented to support the argument that the claimed genus is a large and variable genus.

13. Applicant's arguments have been fully considered but are not deemed persuasive. In regard to the recent decision in *Boehringer Ingelheim Vetmedica, Inc. v. Schering Plough Corporation*, 65 USPQ2d 1961 (CA FC 2003), it is noted that the issue being discussed in the instant rejection is not equivalence, which is the issue which was discussed in *Boehringer Ingelheim Vetmedica, Inc. v. Schering Plough Corporation*. In fact, the statement quoted by Applicants further support the Examiner's argument that even a single amino acid substitution may drastically alter the function of a gene or a protein. In regard to Bork, it is not the Examiner's contention that sequence homology is completely unreliable and that it should never be used to make functional predictions but rather the unpredictability of using solely sequence homology to accurately determine function. As indicated by Bork, while accurate predictions have been made in some cases, Bork also teaches that while gene annotation using structural homology is routine, the error rate is considerable (page 399, second column) as evidenced in Table 1 and that the numbers in Table 1 are overestimates (page 400, first column, last paragraph).

In regard to the irrelevance of Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), Broun et al. (Science 282:1315-1317, 1998) and Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001), it is noted that even if the enzymes described in those references belong to the same general class of enzymes, they are not the same since they catalyze different reactions and/or have different substrates. Furthermore, the relevance of these references is not in regard to whether the polynucleotides claimed encode fatty acyl hydroxylases, desaturases or bacterial amidohydrolases but rather to present state of the art evidence establishing the unpredictability of assigning any function based on sequence homology.

14. **In page 16, part D**, Applicants argue that the state of the art at the time of the present invention is further advanced than at the time of the Lilly and Fiers applications. Applicants argue that the state of the art was at essentially the dark ages of recombinant DNA technology when the Lilly and Fiers applications were filed, whereas the instant application was filed 19 years after, when much has happened in the development of recombinant DNA technology.

15. Applicant's arguments have been fully considered but are not deemed persuasive. While it is agreed that much has happened in the area of recombinant DNA technology since 1977, the state of the art after 1999 as extensively discussed above, teaches the unpredictability of determining function based on structural homology without any teaching or suggestion as to how structure correlates with function.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

16. Claim 31 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 9, does not reasonably provide

enablement for naturally-occurring structural homologs of the polynucleotide of SEQ ID NO: 9 of any function. This rejection has been discussed at length in Paper No. 13, mailed on 2/24/2003.

17. **In page 17, part A**, Applicants argue that the specification teaches how to make the claimed invention. Specifically, Applicants argue that the specification teaches how to isolate naturally occurring homologs in other individuals and species and how to use CLUSTAL V and BLAST to determine whether a naturally occurring polynucleotide having 80% sequence identity to the polynucleotide of SEQ ID NO: 9 falls within the scope of the claim. Also, Applicants argue that the specification teaches how to make the claimed polynucleotides by recombinant and chemical methods.

18. Applicant's arguments have been fully considered but are not deemed persuasive. As indicated above, the structural homologs claimed can have any function. While it is agreed that (1) making 80% structural homologs of the polynucleotide of SEQ ID NO: 9 is not undue experimentation since this is done routinely in the art, and (2) one of the skill in the art would know how to use CLUSTAL V and BLAST, the Examiner disagrees with Applicant's contention that the specification teaches how to isolate the naturally-occurring polynucleotides encompassed by the claims wherein said polynucleotides encode PSST subunits of the NADH:ubiquinone oxidoreductase complex. As indicated above, structural homology alone is not sufficient to accurately predict function. One would require some knowledge or guidance as to how structure correlates with function to determine whether or not naturally-occurring polynucleotides encode PSST subunits of the NADH:ubiquinone oxidoreductase complex, which is the only function disclosed in the specification. Furthermore, while making the structural homologs as recited in

the claim is not undue experimentation, making and testing an infinite number of these homologs and determine which ones encode PSST subunits of the NADH:ubiquinone oxidoreductase complex, without any teaching or suggestion as to which ones are more likely to encode the protein with the desired function, is undue experimentation.

19. **In page 18, part B**, Applicants argue that the specification teaches how to use the claimed invention and submit that the rejection is improper since the claimed invention has patentable utility and/or a utility well known to one of ordinary skill in the art. Applicants assert that the invention at issue is a polynucleotide which corresponds to a gene that is expressed in human bladder tissue as well as variants of the polynucleotide of SEQ ID NO: 9, and that the novel polynucleotide codes for a polypeptide which is a member of the class of PSST subunits of the NADH:ubiquinone oxidoreductase complex. According to Applicants, the claimed invention has numerous uses such as in toxicology testing, drug development and diagnosis of disease, none of which require knowledge of function. Applicants argue that as a result of these benefits of these uses, the claimed invention enjoys significant commercial success. Applicants submit a declaration by Dr. Tod Bedilion, a consultant for Incyte Genomics, which is the assignee of record for the instant application. Applicants indicate that the declaration describes some of the practical uses of the claimed invention in gene and protein expression monitoring and demonstrate that the Examiner's arguments with respect to enablement and utility are without merit. Applicants assert that the Final Office Action Paper No. 13 is replete with new arguments and positions in an attempt to justify the rejections under 35 USC 112, first paragraph. Specifically, the Examiner has presented new arguments and positions in regard to uses of the claimed polynucleotides for gene expression and a new rejection under 35 USC 112 on the basis

of written description. Therefore, applicants are submitting a Declaration in response to the new arguments and positions taken by the Examiner and assert that this is sufficient justification under 37 CFR 1.195 as to why this declaration was not submitted earlier.

20. Applicant's arguments have been fully considered but are not deemed persuasive. It is not the Examiner's contention that the specification fails to teach how to use the polypeptide of SEQ ID NO: 1 or the polynucleotide of SEQ ID NO: 9. While the specification discloses the function of the polypeptide of SEQ ID NO: 1 and its corresponding polynucleotide (SEQ ID NO: 9), the specification is silent in regard to all the functions of structural homologs as encompassed by the claim. As such, the specification fails to teach how to use those structural homologs of any function.

The Examiner disagrees with Applicant's contention that the Bedilion declaration is necessitated by new issues raised by the Examiner in the Final Office Action Paper No. 13, for the following reasons. Applicants submitted arguments in Paper No. 12, filed on 6/12/2002 in regard to the many uses described in the specification for the claimed polynucleotides such as in toxicology testing, drug development and diagnosis of disease. Furthermore, Applicants submitted references by Steiner et al. (Toxicology Letters 112-113:467-471, 2000), Rockett et al. (Xenobiotica 29:655-691, 1999), Nuwaysir et al. (Molecular Carcinogenesis 24:153-159, 1999), Rockett et al. (Environ. Health Perspec. 107:681-685, 1999) as evidence of the state of the art in regard to toxicology testing, its use in the pharmaceutical industry, and the genes/nucleic acids which are incorporated in toxicology testing. Applicants also submitted in Paper No. 12, an e-mail from Dr. Cynthia Afshari to an Incyte employee to support the argument that any gene is relevant for screening of toxicological effects, and examples of Incyte collaborators or customers

who have been able to obtain benefits from the information provided by Incyte's databases. Therefore, it was Applicant and not the Examiner who introduce new arguments in regard to the use of the claimed invention, as evidenced by the references and arguments previously presented in Paper No. 12. The Examiner merely addressed the arguments and issues raised by Applicants. As indicated by Applicants, the Bedilion declaration is submitted in support of the argument that one of skill in the art do not require to know the function of the claimed polynucleotides since these polynucleotides have practical uses in gene and protein expression monitoring. These arguments have already presented by Applicants in previous Paper No. 12. Since the Examiner did not raise new issues as asserted by Applicants and the utility issues raised by the Bedilion declaration have already been presented and addressed in Paper No. 13, the Examiner will not consider the Bedilion declaration.

21. **In pages 21-39**, Applicants extensively argue that the claimed structural homologs have utility. In particular, Applicants argue that the claimed polynucleotides can be used for diagnosis of conditions and disorders, for toxicology testing and for drug discovery. Applicants resubmit the references described above and further submit a reference by Lashkari et al. (Proc. Natl. Acad. Sci. USA 94:8945-8947, 1997), which according to Applicants, teaches that predicted open reading frames (ORF) have numerous uses, including being applied onto glass for expression analysis. According to Applicants, these uses are sufficient to satisfy the 35 USC 101 utility requirement and they are well-established. Applicants submit that the similarity of the polypeptides encoded by the claimed polynucleotide to another polypeptide of known utility should demonstrate utility. Applicants assert that the rejection is without merit and submit that the precise biological role or function is not required to demonstrate utility. Applicants submit

that requiring Applicants to assert a particular or unique utility is misstating the law and that the Utility Guidelines cannot be applied consistently with the law.

22. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. It is noted that the structural homologs as recited in the claim having the function disclosed in the specification are not being rejected for lack of utility. The enablement rejection is being applied to the claimed polynucleotides of any function in view of the fact that the functions of those polynucleotides have not been disclosed, therefore one of skill in the art would not know how to use them. Applicant's references by Rockett et al., Lashkari et al., Nuwaysir et al., Rockett and Dix, Steiner et al. and the e-mail by Dr. Cynthia Afshari (Incyte employee) have all been reconsidered but are not found persuasive. As indicated previously, arguments in regard to the use of the claimed polynucleotides for diagnosis and disorders, for toxicology testing and for drug discovery are not enabled by the instant specification due to the fact that the specification is silent in regard to the biological function or role of the claimed polynucleotides and does not provide any information as to the diseases or disorders which are associated with said polynucleotides. While one could argue that the precise biological role is not required, it is noted that the specification provides no information as to (1) whether diseases or disorders are associated with the expression of said polynucleotides or lack thereof, or (2) the level of expression which is indicative of the disease or disorder. Moreover, as already discussed in the Final Office Action Paper No. 13, while polynucleotides can be used to examine differential gene expression for drug discovery and toxicology testing, it is unclear as to how one can use the instant polynucleotides as asserted if the specification does not disclose any correlation between the expression of the instant polynucleotides and any specific particular

biological function. One of skill in the art would require to know (1) which condition is going to be treated with the drug being tested or (2) which is the biological function which is being affected by the compound used in toxicology testing.

In regard to arguments that the similarity of the polypeptides encoded by the claimed polynucleotide to another polypeptide of known utility should demonstrate utility, it is noted that the references cited by the Examiner in previous Office Action Paper No. 13 as well as the discussion above demonstrate that unless some structure/function information is provided, assigning biological function based solely on sequence homology is unpredictable and it would constitute undue experimentation to determine the actual function without any guidance as to the relationship between structure and function. In regard to Applicant's assertion that the Utility Guidelines cannot be applied consistently with the law, it is noted that the Examiner must use the USPTO Guidelines in the examination of the instant application and cannot use her own interpretation of patent law.

Claim Rejections - 35 USC § 102

23. Claim 31 was rejected under 35 U.S.C. 102(b) as being anticipated by Hyslop et al.

24. This rejection is hereby withdrawn in view of Applicant's amendment of claim 31 which now recites "80% identical to the polynucleotide sequence of SEQ ID NO: 9 over the entire length of SEQ ID NO: 9". The polynucleotide of Hyslop et al. is 648 nucleotides long and presents 3 mismatches. The polynucleotide of SEQ ID NO: 9 is 824 nucleotides long. As such, the polynucleotide of Hyslop is 78.3% [=(648-3)*100/824] sequence identical over the entire length of SEQ ID NO: 9.

Conclusion

25. The rejections previously applied are, therefore, maintained for the reasons of record and the reasons set forth above.

26. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: 3-6 and 8

Claims(s) objected to: NONE

Claim(s) rejected: 31

Claim(s) withdrawn from consideration: 10-14, 23, 26-30, 32-36

27. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

28. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
June 19, 2003

REBECCA E. PRUTY
PRIMARY EXAMINER
GROUP ~~1600~~ 1600